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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/668,168	09/24/2003	Krista Evans	0942.402003	5379
26111	7590	10/04/2005		
STERNE, KESSLER, GOLDSTEIN & FOX PLLC 1100 NEW YORK AVENUE, N.W. WASHINGTON, DC 20005			EXAMINER SLOBODYANSKY, ELIZABETH	
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 10/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/668,168

Applicant(s)

EVANS, KRISTA

Examiner

Elizabeth Slobodyansky, PhD

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 July 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 24 September 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>2nd IDS of 7/9/04, page 2.</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The amendment filed July 13, 2005 amending claim 1 and adding claims 2-22 has been entered.

Claims 1-22 are pending.

Information Disclosure Statement

Document AL2 (WO 02/085936) on page 2 of Second Supplemental IDS filed July 9, 2004 was inadvertently not initialed. The reference was considered and page 2 with all the references initialed is attached hereto.

Drawings

It is noted that the complete set of drawings filed September 24, 2003 (Figures 1-12) is present in the file.

Claim Objections

Claims 1 and 15 are objected to because of the following: "alanine" at position 64 is recited twice and "aspartic acid" and "glutamic acid" should be recited instead of "aspartate" and "glutamate".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 8-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 has been amended to include limitation "if said residue at position 64 is leucine then said residue at position 65 is not alanine, glycine". New independent claim 15 contains the same limitation. Claims 8-14 depend from claim 1. claims 16-22 depend from claim 15. The Examiner is unable to locate adequate support in the specification for such limitation. Thus there is no indication that GFP mutants which meet said limitation were within the scope of the invention as conceived by Applicants at the time the application was filed.

Accordingly, Applicants are required to cancel the new matter in the response to this Office Action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cormack et al.

This rejection is over mutant GFPs that differ from the wild type *A. victoria* GFP by mutations at positions 64 and 65. Such mutants are enabled and are not included in the enablement rejection above.

Cormack et al. (US Patent 5,804,387, form PTO-1449 filed July 9, 2004, reference AD1) teach that "Mutants with Ala, Gly, Ile, Cys or Thr substituted for Ser65 had large shifts in excitation maxima, and fluoresced more intensely than wild-type protein when excited at 488 nm" (column 2, lines 22-25). They further teach that "The mutation of Ser65 to Thr or Cys was observed to increase by a factor of 6 the fluorescence of GFP following 488 nm excitation" (column 2, lines 44-46, and Table 1).

Cormack et al. teach a set of mutations at positions comprising S65 and F64 (column 3, lines 1-3). They teach that "the set of positions consists of all amino acid positions in the mutant GFP in which an amino acid differs from the corresponding amino acid of wild-type GFP" (column 3, lines 3-6). They explicitly teach GFP mutant F64L/S65T (GFP mut1) and DNA encoding thereof that has enhanced fluorescence

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compared with the wild type GFP and a single mutant (abstract; Figures 4-5; column 9, Table 4). They teach vectors, host cells comprising DNA encoding such GFP mutants and methods for producing said mutants.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce double GFP mutants comprising S65A, S65T or S65C coupled with any amino acid substituted for F64 as suggested by Cormack et al. One of ordinary skill in the art would have been motivated to do so in order to find double 64/65 GFP mutants that have similar or different fluorescent properties because such mutants can be used for protein localization and trafficking. One of ordinary skill in the art would have a reasonable expectation that other double 64/65 GFP mutants with possible slight variations would have useful fluorescent properties. Therefore, mutants such as A2, A5, A8 and A9 are considered obvious (claims 2-7). Furthermore, testing of even all possible 64/65 GFP mutants does not require undue experimentation in view of the limited number of the double 64/65 GFP mutants that can be made.

Claims 15-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cormack et al. in view of Zolotukhin et al.

The teachings of Cormack et al are outlined above.

Zolotukhin et al. (form PTO-1449 filed July 9, 2004, reference AS8) teach humanized cDNA encoding wild-type GFP and S65T mutant thereof (page 4649, 1st column, last full paragraph). The humanized DNA enhances the efficiency of translation and hence expression up to 22-fold in mailman cells. In addition, a S65T mutation in

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humanized GFP DNA results in 5 to 10 fold increase over humanized wild-type (page 4649, Figure 3).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce double F64/S65 GFP mutants suggested by Cormack et al using humanized cDNA taught by Zolotukhin et al. One of ordinary skill in the art would have been motivated to do so in order to achieve high-level expression in mammalian, including human, cells.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 and 8-22 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-22 of U.S. Patent No. 6,638,732. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-12 and 14-22 of U.S. Patent No. 6,638,732 are drawn to a DNA encoding SEQ ID NOs:5 and 6 and a humanized DNA

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encoding SEQ ID NOs:5 and 6, vectors, host cells and kits comprising thereof and methods for producing a mutant GFP. Claims 1 and 8-22 are generic to all that is recited in claims 1-12, 14-22. Thus, claims 1-12 and 14-22 of US Patent No. 6,638,732 fall entirely within the scope of claims 1 and 8-22. In other words, claims 1 and 8-22 are anticipated by claims 1-12 and 14-22 of US Patent No. 6,638,732.

Response to Arguments

Applicant's arguments filed July 13, 2005 have been fully considered but they are not persuasive.

The 112, 1st paragraph, written description and enablement, and 112, 2nd rejections are withdrawn in view of the amendment. The current claims are drawn to or depend from a DNA encoding a GFP mutant that differs from the wild-type GFP at positions 64 and 65.

The 102(b) rejection over Delagrave et al is withdrawn in view of the amendment. Delagrave et al. (form PTO-1449 filed July 9, 2004, reference AR3) teach a DNA encoding GFP mutant F64L/S65L RSGFP2. said mutant in addition to F64L/S65L contains mutation V68A (page 152, Table 1).

With regard to the 103(a) rejection over Cormack et al., Applicants argues that "The Examiner asserts that it would have been obvious to one of ordinary skill in the art at the time the invention was made to produce double GFP mutants comprising S65T or 565A coupled with any amino acid substituted for F64. Applicant disagrees that these modifications, and in particular the mutants at positions 64 and 65 recited in claim 1, are

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disclosed in Cormack " (page 14, 1st paragraph). it is agreed that the mutations of claim 1 are not disclosed in Cormack but the rejection is 103(a) not 102. As a reference in the 103(a) rejection, that reference does not have to disclose the same invention but only to make it obvious.

Applicant further argues that "Cormack does not provide motivation for making the set of mutations set forth in present claim 1" (page 14, 2nd paragraph). This is not found persuasive for the reasons explained above in the rejection. Specifically, Cormack provides motivation to make any combination of double F64/S65 mutations. These mutations comprise mutations recited in claim 1.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

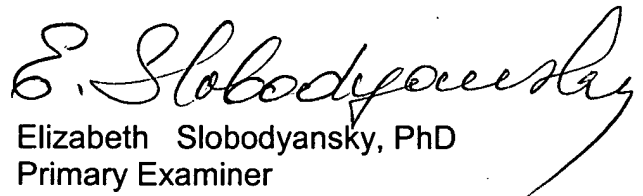
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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky, PhD whose telephone number is 571-272-0941. The examiner can normally be reached on M-F 10:00 - 6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, PhD can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Elizabeth Slobodyansky, PhD
Primary Examiner
Art Unit 1652

September 22, 2005